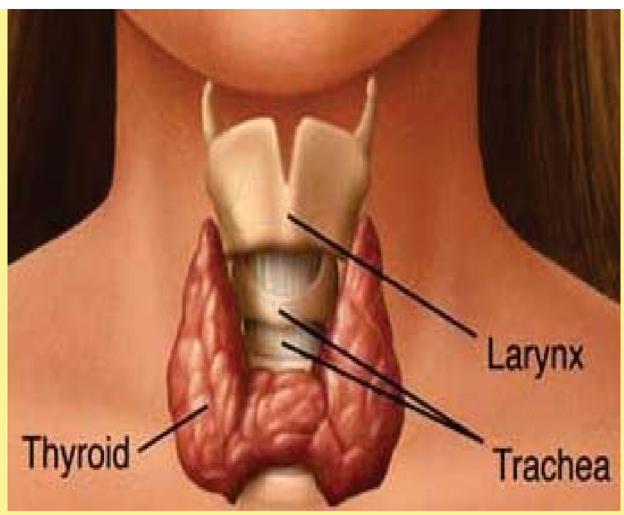
THE REST OF THE STORY

THYROID GLAND

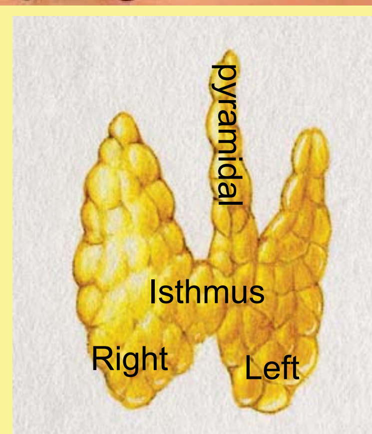
The endocrine secretions of the thyroid are involved in:

1. regulation of tissue metabolism
2. regulation of tissue growth
3. 2nd regulation of plasma Ca++



DEVELOPMENT & ORGANIZATION

- **The thyroid gland consists of 2 lateral lobes of endocrine tissue connected by a narrow isthmus laying over the 2nd and 3rd tracheal rings.**
- **Frequently a medial "pyramidal lobe" is present which extends upward towards the larynx.**

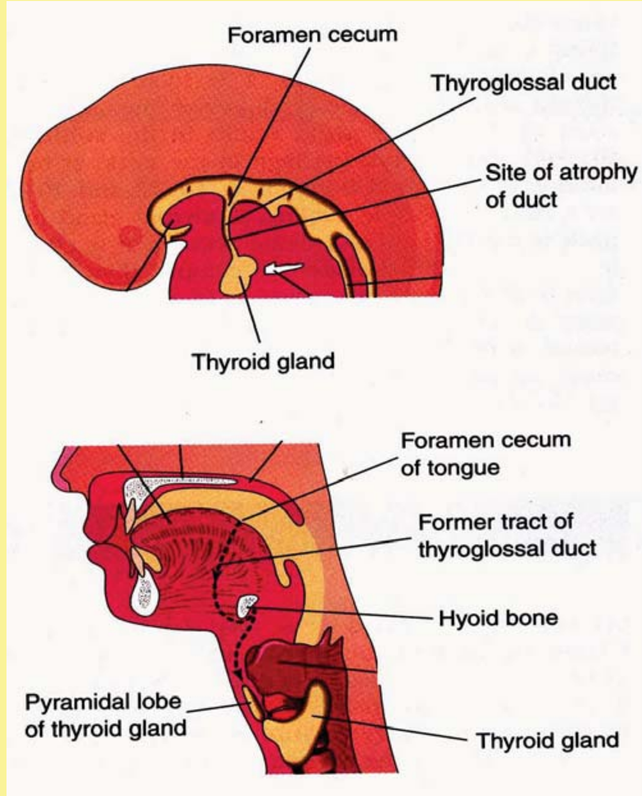


- Embryologically - develops from a median downgrowth of the base of the tongue -- descends to the upper tracheal region along a stalk-like attachment = the *Thyroglossal Duct*

- *This duct is usually obliterated during development and is rarely present in adults.*

- The parenchyma of the thyroid is enclosed externally by a layer of dense irregular connective tissue.

- Beneath this outer connective tissue sheath lies a thin inner connective tissue capsule which penetrates the lobes of the gland, dividing them into poorly delimited lobules



FUNCTIONAL UNIT

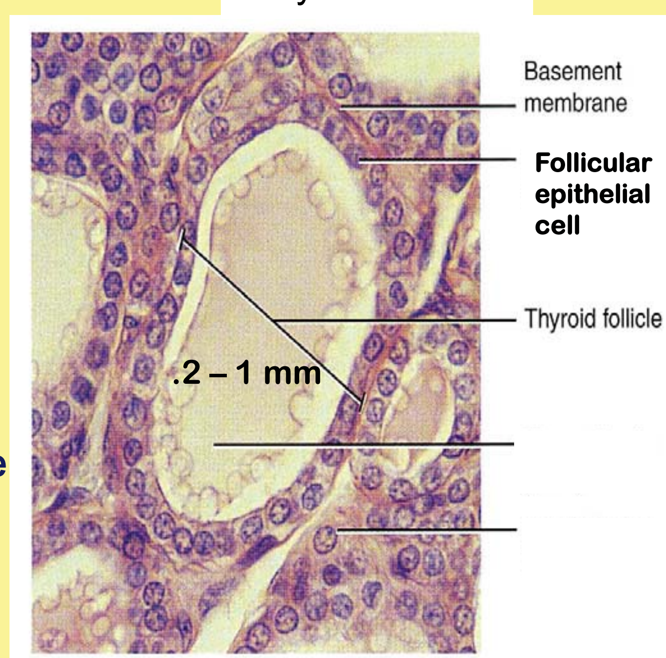
Ž **The lobules of the thyroid gland are composed of spherical cyst-like FOLLICLES**

Ž **Enclosed by a single layer of simple cuboidal epithelial cells = *FOLLICULAR EPITHELIAL CELLS*.**

- Follicles range from .2 - 1.0 mm

Each follicle is surrounded by a thin Basal Lamina supported by a delicate network of reticular fibers.

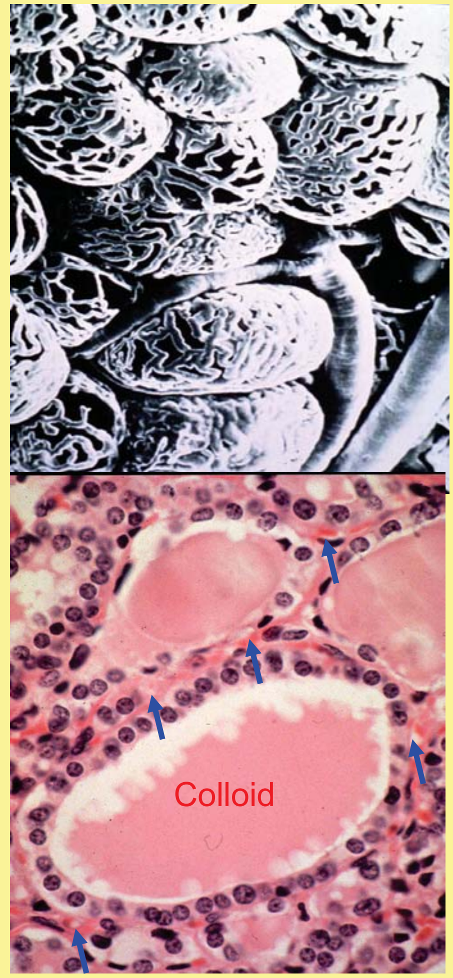
Thyroid Follicle



Each follicle is also enveloped by a dense basket-like meshwork of fenestrated capillaries into which the endocrine secretion is emptied. Between follicle are lymphatic vessels

The center of each follicle is filled with a homogeneous gelatinous substance = *COLLOID* which is the stored product of the surrounding epithelial cells.

The follicle represents both the structural and functional subunit of the thyroid gland.



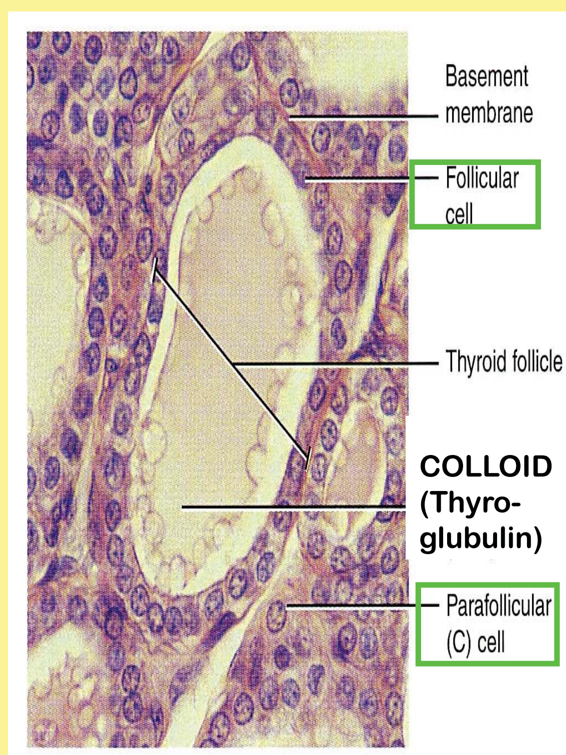
CELLS OF THE THYROID:

Thyroid follicles are composed of 2 classes of cells:

1. Follicular Epithelial Cells - also called "Principal Cells"

2. Parafollicular Cells - also called "C-cells"

Thyroid Follicle



THYROID FOLLICULAR CELLS

Epithelial cells arranged in a continuous ring around the follicle.

-- Cytoplasm is slightly basophilic with a round, centrally located nucleus

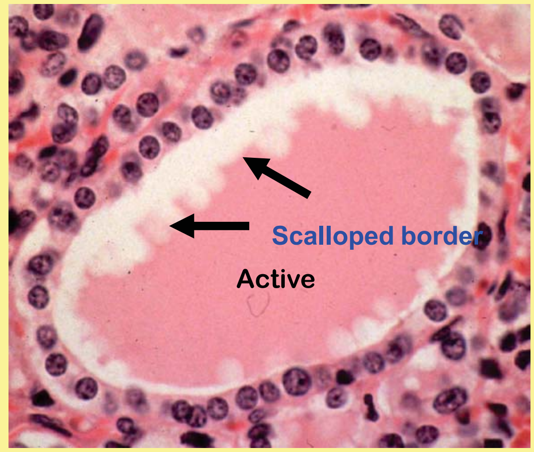
Typically follicular cells are __simple cuboidal cells__ but their shape can vary depending upon the state of activity of the gland.

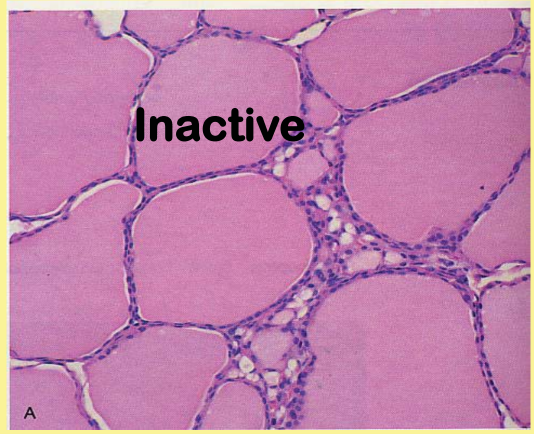
Hyperactive:

epithelial cells become active and take on a "cuboidal-columnar" shape -- colloid is reduced in follicle often exhibiting a "__scalloped border__"

Hypoactive:

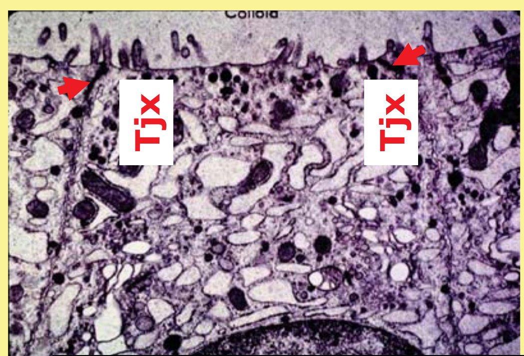
epithelial cells are inactive and assume a "squamous" shape -- colloid is increase in follicle.

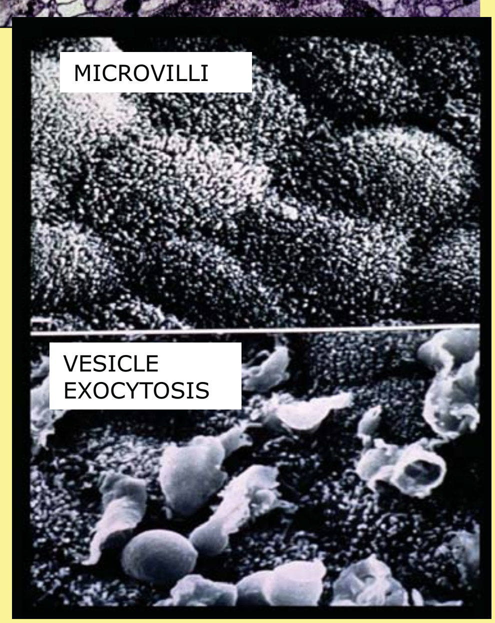




At the EM level: ultrastructural features of a cell producing protein for export

- -- __Tight junctions__ - desmosomes and gap junctions -- at the lateral borders between follicular cells
- -- dilated cisternae of RER, scattered ribosomes
- -- distended Golgi apparatus
- -- colloid droplets
- -- scattered __Lysosomes__
- -- numerous __coated vesicles__
- -- __microvilli__





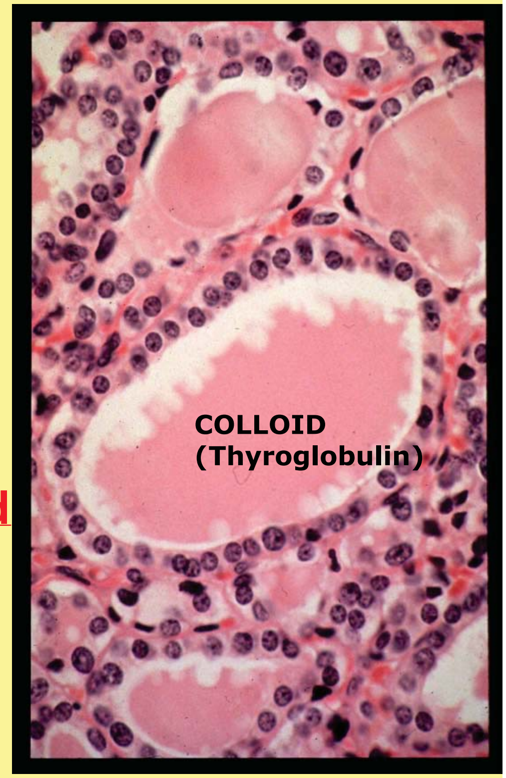
Major Function: = synthesis and excretion of *THYROID HORMONE*.

Thyroid Hormone is synthesized from a precursor glycoprotein *THYROGLOBULIN*

COLLOID =
primarily *THYROGLOBULIN* produced by the follicular cells and exocytosed into the lumen.

Thyroglobulin is stored in the lumen of the follicle in the form of iodinated thyroglobulin until the thyroid gland is activated

Follicular cells are unique among endocrine cells --- they are the only endocrine cells that store their product extracellularly



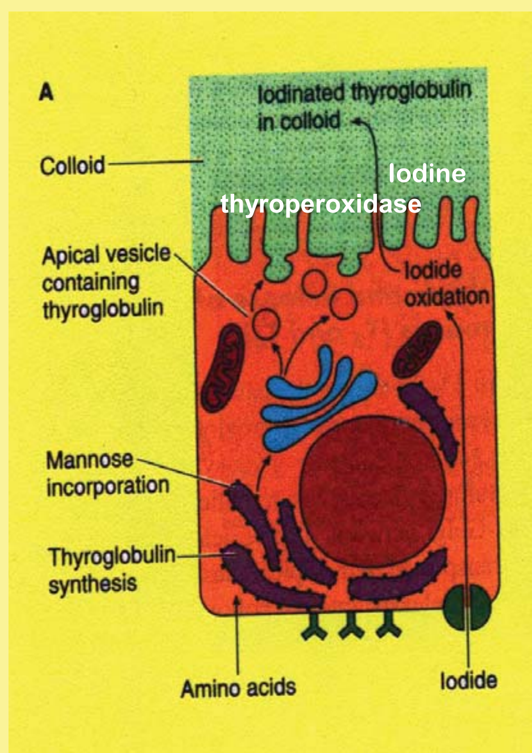
The Synthesis of Thyroid Hormone from Thyroglobulin

1. Thyroglobulin --- synthesized in the rER of the follicular cells and processed in the golgi apparatus.

2. Tyrosine residues are added to the thyroglobulin skeleton and the compound is the shipped via vesicles to the apical surface of the cell where it is exocytosed into the lumen.

3. The enzyme *THYROPEROXIDASE* is produced by the follicular cells and secreted into the lumen.

   This enzyme catalyses the iodination of Thyroglobulin in the lumen of the follicle in close approximation (1-2µm) to the microvilli at the apical surface of the cells.



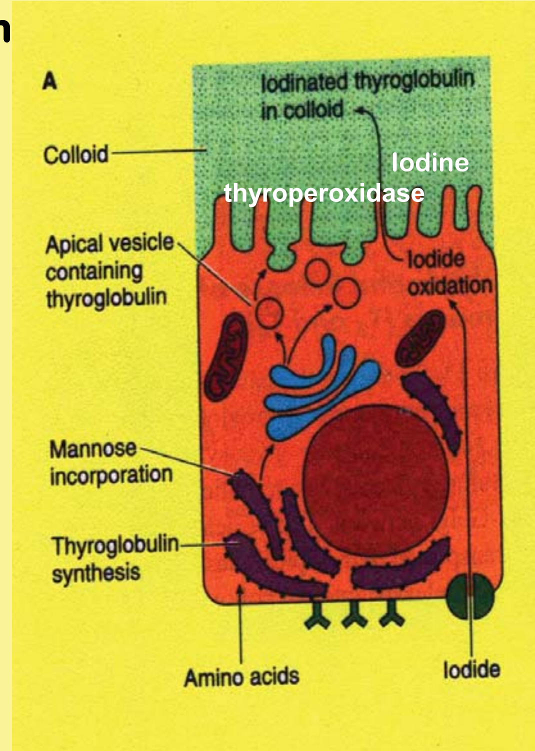
4. - iodide is sequestered from the plasma through an "iodide pump" in the basal plasma membrane of the follicular cells.

- iodine, for the iodination of thyroglobulin is produced from the oxidation of iodide

5. iodine is excreted into the follicular lumen

6. Thyroglobulin is iodinated, producing a series of iodinated residues on the thyroglobulin molecule:

-- Mono-iodotyrosine (MIT)
-- Di-iodotyrosine (DIT)
-- Tri-iodothyronine = { MIT + DIT }= T3
-- Tetra-iodothyronine = {DIT + DIT}= T4 or Thyroxine

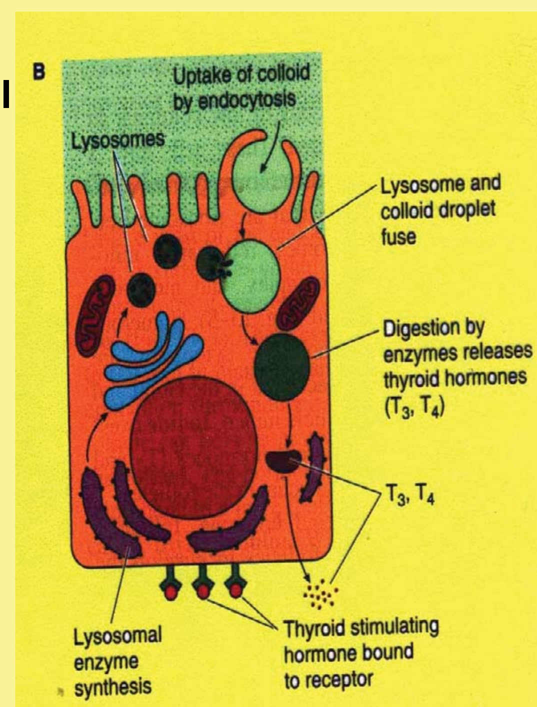


7. Reuptake of iodinated thyroglobulin at the apical surface to form colloid droplets

8. Inside the cytoplasm of the follicular cell the iodinated thyroglobulin is subjected to "lysosomal digestion". This proteolysis results in the production of free T3 and T4 and MIT and DIT

-- T3 and T4 represent the active forms of Thyroid Hormone.

-- MIT and DIT serve as iodine carriers and are de-iodinated in the cytoplasm and reserved for recycling.



9. T3 and T4 diffuse out of the "basal" surface of the follicular cell and enter the capillary circulation. Once in the circulation they are bound to a plasma proteins on their way to target tissues.

Ž Activation of the thyroid gland is under the influence of thyroid stimulating hormone (TSH) released from the basophilic thyrotrophs of the anterior pituitary

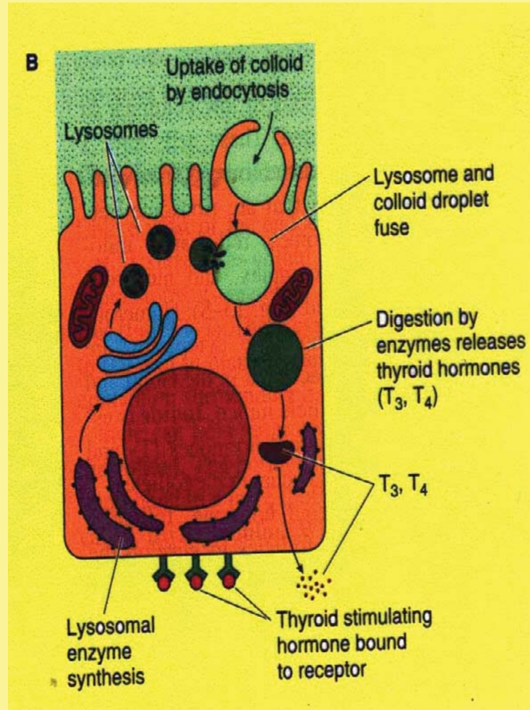
Ž TSH binds to receptors on the basal surface of the follicular cells and causes

– hypertrophy and hyperplasia of the follicular cells

– increased production & iodination of thyroglobulin

– increased re-uptake and lysosomal digestion of iodinated thyroglobulin

– increased secretion of T3 and T4



THYROID HORMONE REGULATION:

— Plasma levels of T3/T4 are monitored by neurosecretory neurons in the hypothalamus.

— Low levels of T3/T4 in the blood initiate a cascade of events leading to upregulation of thyroid hormone secretion:

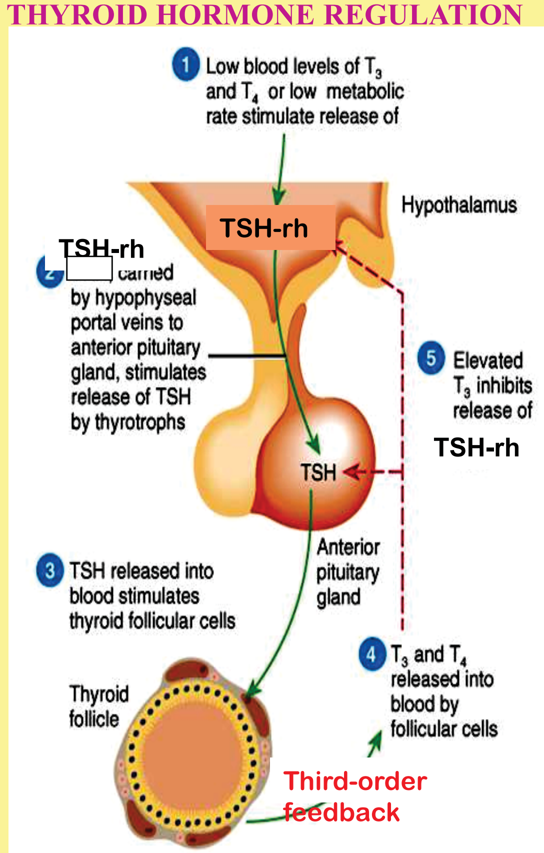
1. TSH releasing hormone is released into the hypothalamic hypophyseal portal system by neurosecretory cells in the basal hypothalamus

2. TSHrh stimulates TSH release from anterior pituitary thyrotrophs into the systemic circulation

3. The follicular cells respond to increased TSH levels by increasing the synthesis and secretion of T3/T4.

4. Increased T3/T4 levels in the blood, feed back to the hypothalamic neurosecretory cells to downregulate TSHrh release.

THYROID HORMONE REGULATION



THYROID HORMONE FUNCTION:

Thyroid hormone is concerned primarily with cellular metabolism in all body tissues. Its effects are complex and can be divided into two general categories:

1. Metabolic Effects
2. Growth Promoting Effects

1. Metabolic Effects:

Calorigenisis - increased energy production and oxygen consumption (Basal Metabolic Rate)

BMR = kilocalories expended / square meter of body surface area / hour

Measure of energy expenditure & cellular metabolism at rest
(accounts for 60%-70% of normal energy expenditure)

BMR - increases with exercise and fitness
- decreases with dieting and age

Regulation of water and ion transport

Regulation of protein, fat and carbohydrate metabolism

2. Growth Promoting Effects:

Acts synergistically with Growth Hormone to promote normal skeletal development.

Controls "molting" and "metamorphosis" in lower vertebrates

THYROID DYSFUNCTION:

Alterations in thyroid function lead to a variety of physiological changes.

HYPOTHYROID	HYPERTHYROID
-- Mentally & physically sluggish	--restless, irritable anxious
-- Low BMR	-- elevated BMR
-- mental retardation	-- mentally alert
-- decreased glucose absorption in GI tract	-- increased glucose absorbtion in GI tract
-- weak heart beat	-- tachycardia

BMR = calories / kilogram of bodyweight / hr

CLINICAL CONSIDERATIONS

Hypothyroidism:

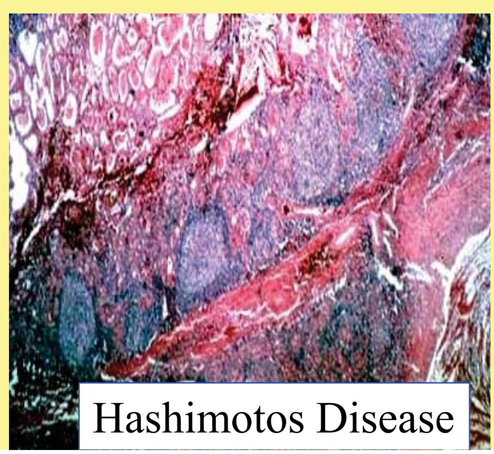
during development leads to a condition characterised by a stunting of physical and mental development known as CRETINISM

in adulthood results in a condition characterised by lethargy, and mental deficiency, known as MYXEDEMA.

hypothyroid symptoms can develop in rare instances from an auto-immune response to thyroglobulin known as HASHIMOTO'S DISEASE
(auto-immune destruction of follicular cells)

CRETINISM

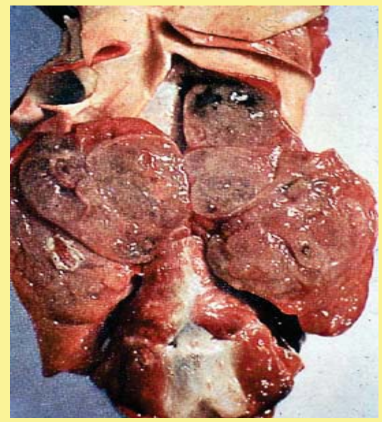
3 CRENTINOUS PATIENTS W/ A NORMAL MALE (ALL AGE 15-20)



Hashimotos Disease

GOITER: Enlargment of the thyroid gland resulting from hypertrophy and hyperplasia of the follicular cells. this condition results from:

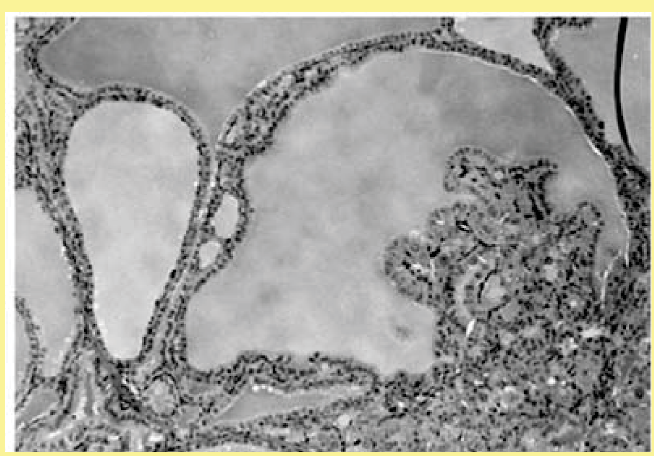
1. **IODINE DEFICIENCY:**
   leading to decreased T3/T4 output, which signals increased TSH release by the pituitary, resulting in compensatory follicular cell hypertrophy (parenchymatous goiter)



2. **GRAVES DISEASE:**
   direct stimulation of follicular cells by a poorly understood plasma IgG termed "thyroid stimulating immunoglobulin". A secondary symptom of this condition is a mark protrusion of the eyeballs = **EXOPTHALMOS**

Exopthalmos
Due to increased water absorbsion in retro-occular orbital tissues

- Follicular cell hypertrophy
- Follicle enlargement
- Increase T3 _T4 levels



PARAFOLLICULAR CELLS (C-cells)

The second, less numerous, cell type found in the walls of the thyroid follicles.

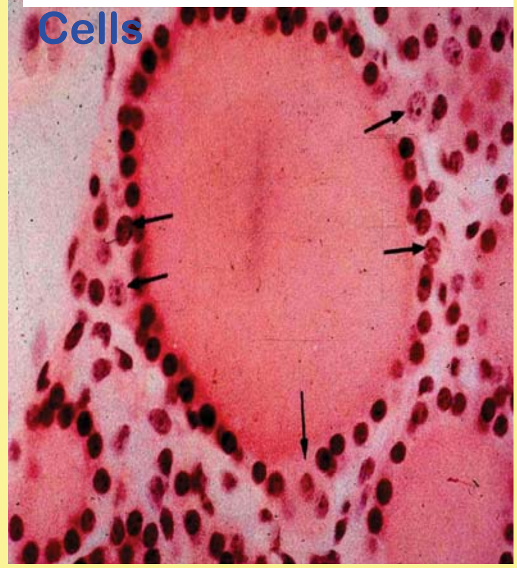
These are of neural crest origin and migrate into the thyroid during development and are considered part of the APUD cell line.

-- larger and lighter staining than follicular cells with a spherical - centrally located nucleus - found between and within follicles.

-- They are invested in the same basement membrane as the follicular cells but are insulated from the lumen (and the colloid) by thin cytoplasmic extensions of the follicular cells

-- cytoplasm exhibit numerous small (100-200nm) vesicles containing the peptide hormone *CALCITONIN*.

Parafollicular "C" Cells



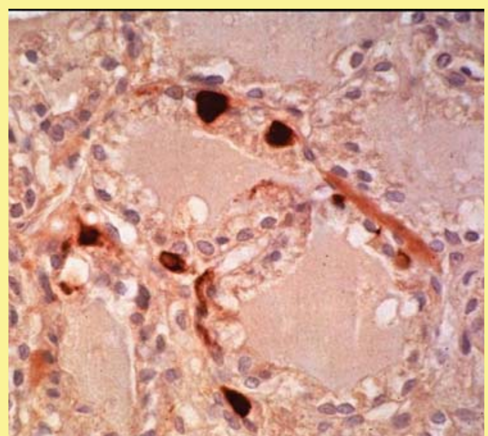
CALCITONIN (Thyrocalcitonin)

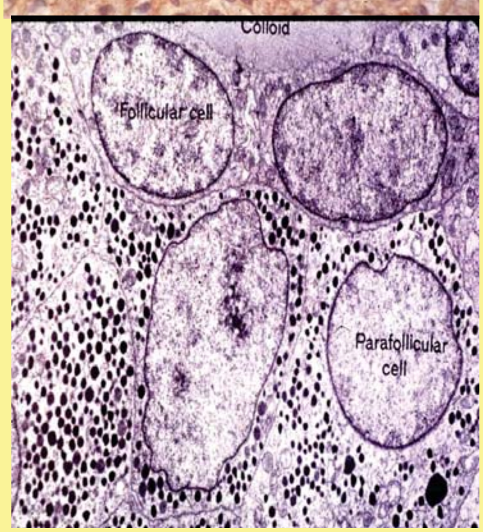
32 amino acid peptide

Calcitonin plays a role in lowering plasma Ca^{++} levels by:

1. inhibiting osteoclast activity and number -----> decreasing bone resorption and the liberation of Ca^{++}
2. promoting excretion of Ca^{++} from the kidneys

Calcitonin is released in direct response to elevated plasma Ca^{++} levels (i.e not under pituitary control).





Parathyroid Glands

CALCIUM REGULATION AND THE PARATHYROID GLAND

The human body contains more Ca^{++} (1200-1400gm) than any other single cation, approx 99% of which is present in the mineral crystals (hydroxyapatite) of bone.

Although the concentration of Ca^{++} ions in plasma (10 mg per 100 ml) is relatively low, Ca^{++} plays a vital role in:

- -- membrane permeability and excitability in muscles and nerves
- -- enzyme activity
- -- receptor binding
- -- blood clotting
- -- maintenance of acid/base balance

Ca^{++} is absorbed primarily through the small intestine an action which is facilitated by a hydroxylated vitamin D derivative *1,25-dihydroxycholecalciferol*

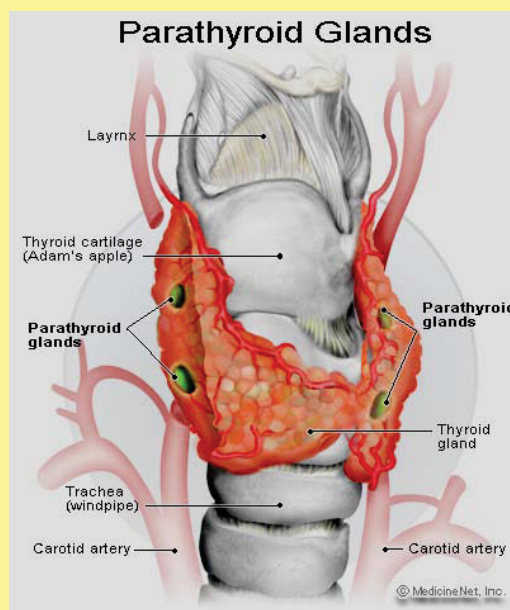
Minor fluctuations in plasma concentration of ionized Ca^{++} can produce dramatic functional alterations:

A. Elevated Plasma Ca^{++} = Hypercalcemia
- -- ectopic calcification of soft tissues
- -- kidney stones

B. Depressed Plasma Ca^{++} (< 9mg/100ml plasma) = Hypocalcemia
- -- hyperexcitability of neurons
- -- prolonged skeletal muscle contractions (tetany)
- -- aberrant cardiac muscle contraction and rhythmicity

PARATHYROID GLAND:

Maintenance of appropriate plasma concentrations of Ca^{++} is under the control of the *PARATHYROID GLANDS*.



Composed of 4 small glandular masses (3 X 6mm) weighing about .4gm situated behind the thyroid gland.

A pair of parathyroid masses is located at each end of the upper and lower portions of the thyroid lobes.

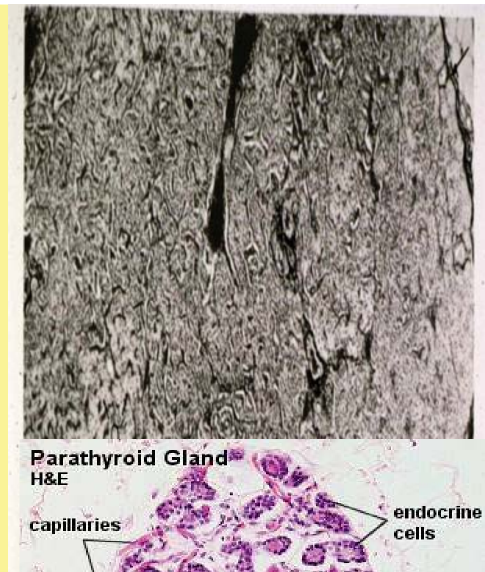
2 Inferior Parathyroids – derived from the 3rd pharyngeal pouch – descend with the thymus

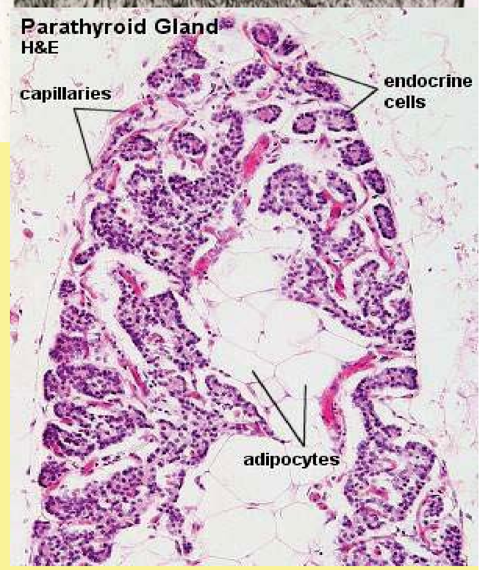
2 Superior Parathyroids – derived from the 4th pharyngeal pouch – descend with the thyroid

The parathyroids lie **immediately external to the true thyroid capsule** but are enclosed in the same external fascia.

The parathyroid is **encapsulated by connective tissue** - connective tissue "septa" carry blood vessels into the tissue but do not separate the glandular tissue into lobes.

Cell of the parathyroid are arranged in large **clumps or cords** supported by **reticular fibers**, separated by wide fenestrated capillaries.





PARATHYROID CELLS:

2 types of cells are found in the parathyroid glands:

CHIEF CELLS (principal) — OXYPHIL CELLS

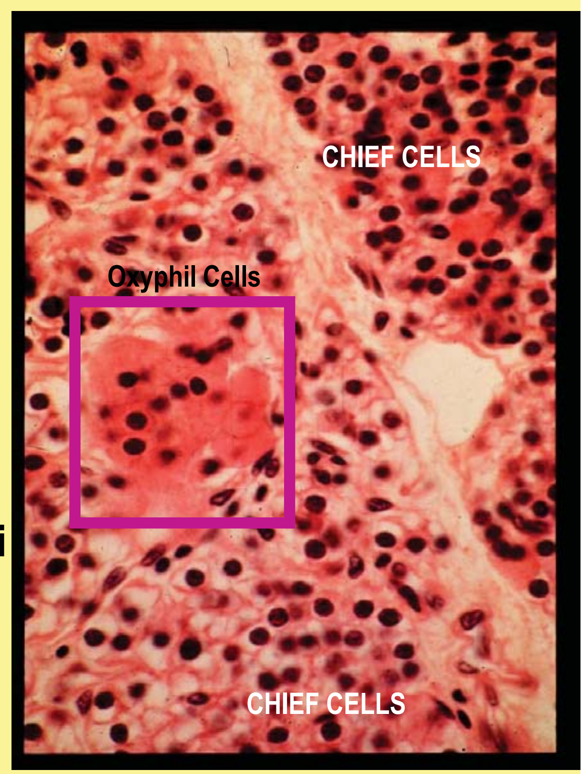
CHIEF CELLS:

These cells secrete PARATHYROID HORMONE, an 84 amino acid peptide formed from the cleavage product of a larger (114 AA) prohormone = pro-parathyroid hormone.

Parathyroid hormone has a half-life of only about 18 minutes in systemic circulation.

- most numerous cell type in the parathyroid
- Small (7-10μm) cells - centrally located nuclei
- clear staining cytoplasm, but 2 distinct forms have been identified

a. light cells = inactive cells
b. dark cells = active PTH secreting cells

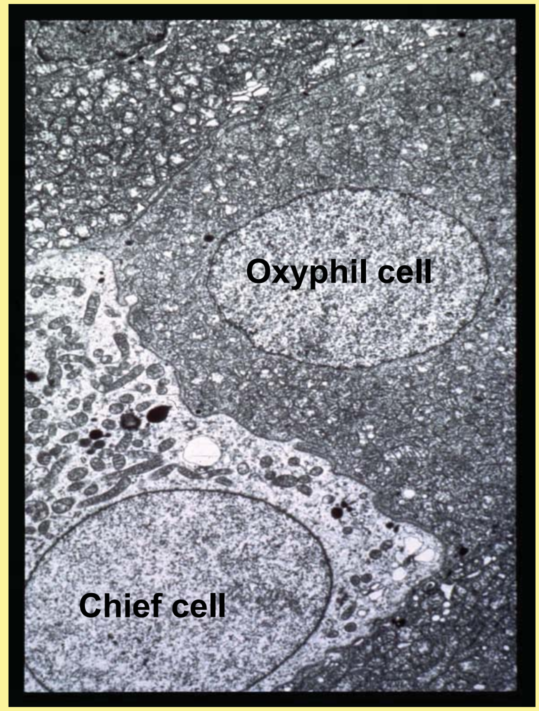


At the EM level

-- well developed ER and Golgi

-- irregularly shaped 200-400 nm secretory granules containing Parathyroid Hormone (84 amino acid peptide)

-- secretory granules are less numerous than in other endocrine cells since Chief cells do not store large quantities of PTH



In response to low plasma Ca^{++} concentration, PTH is released into the circulation by the chief cells. PTH has 3 major plasma-calcium elevating effects

1. Increases release of osteoclast stimulating factor in bone, which stimulates osteoclast activity to increase bone resorption and Ca^{++} release.

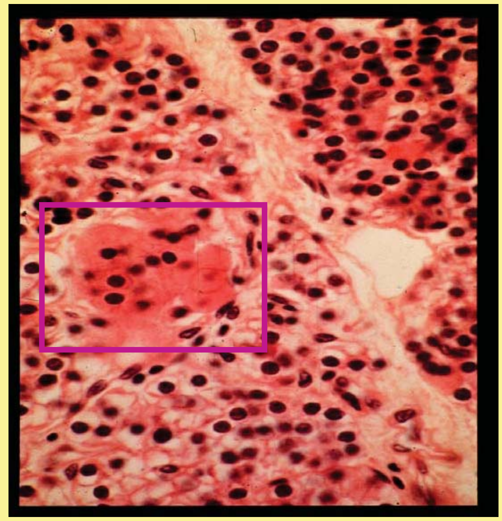
2. Promotes Ca^{++} resorption by the distal convoluted tubules of the kidneys.

3. promotes synthesis of 1,25-dihydroxycholecalciferol, a vitamin D derivitive which facilitates calcium absorption in the small intestine.

The rate of PTH secretion from the chief cells is directly controlled by the plasma concentration of Ca++.

(i.e. not under pituitary control).

OXYPHIL CELLS



The second class of cells comprising the parathyroid gland is the oxyphil cells

-- less numerous than Chief cells

-- larger cells with small darkly staining nuclei

-- cytoplasm is strongly acidophilic

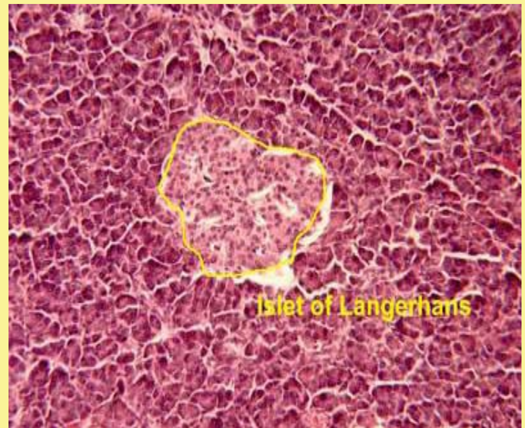
-- these cell do not appear in the gland until about age 7

-- the function of oxyphil cells is unknown, they are not hormone secreting and some investigators feel that they may differentiate from chief cells.

-- At the EM level the cytoplasm of these cells appear filled with NUMEROUS MITOCHONDRIA - *"Bag of Mitochondria"*

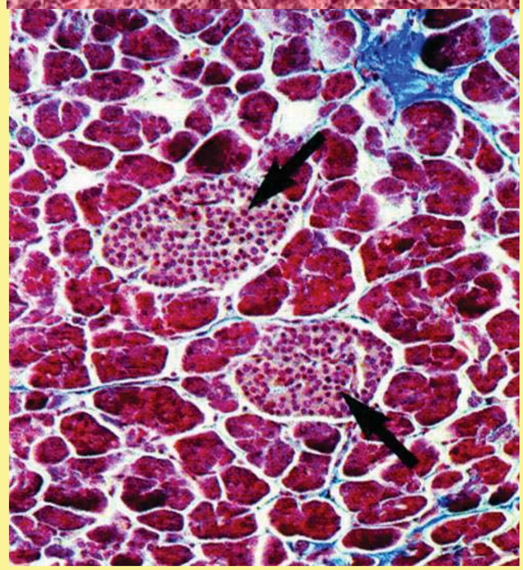
Pancreatic Islets of Langerhans

ISLETS OF LANGERHANS: THE ENDOCRINE PANCREAS



The Islets of Langerhans are multihormonal endocrine micro-organs situated within the parenchyma of the pancreas among the pancreatic acini.

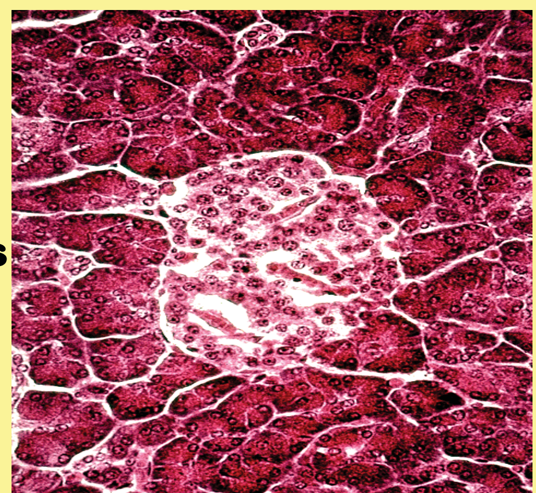
The Islets consist of small clusters (100- 200 µm diameter) containing up to several hundred endocrine cells which appear more concentrated in the tail region of the pancreas.



Islet cells secrete several hormones primarily involved in

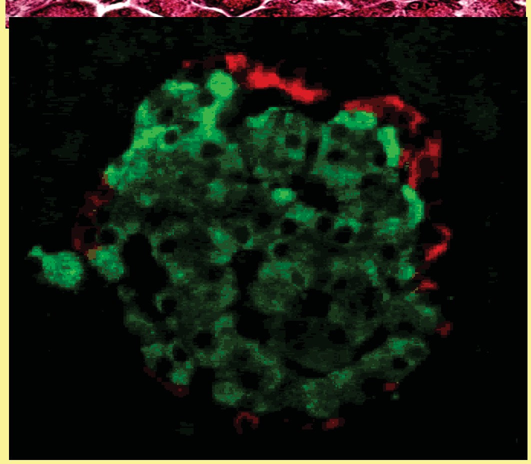
- stimulation of digestion
- regulation of glucose transfer

It is estimated that there may be up to 1 million islets in the human pancreas accounting for about 1-2% of the pancreatic tissue.



The cells of the pancreatic islets are arranged in cords, separated by a dense network of fenestrated capillaries.

Each islet is encapsulated by a delicate network of reticular fibers which support the parenchymal cells and separate them from the surrounding pancreatic acini.

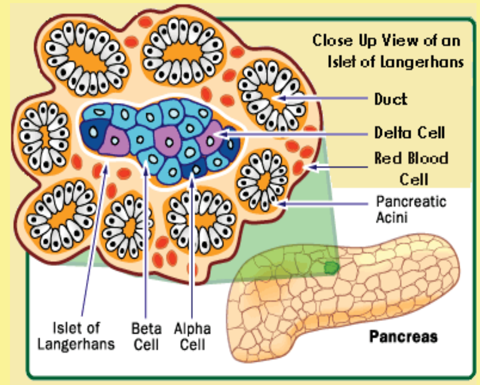


The cells of the islets are pale and somewhat smaller than those of the acini.

Islet Cells

To date 4 distinct cell types have been identified in the pancreatic islets using immunocytochemical markers:

Alpha -- Beta -- Delta -- F cells *(G cells ??)*

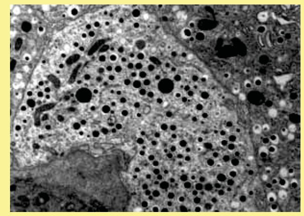


1. ALPHA CELLS: (20%)

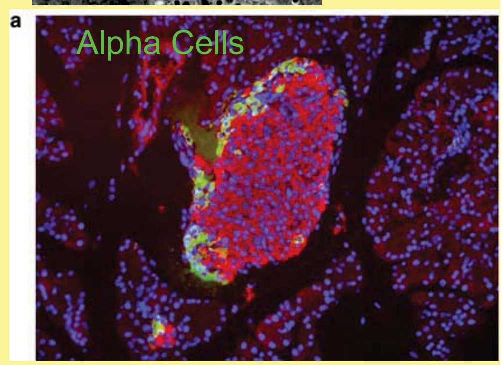
-- large cells

-- located at the periphery of the islet.

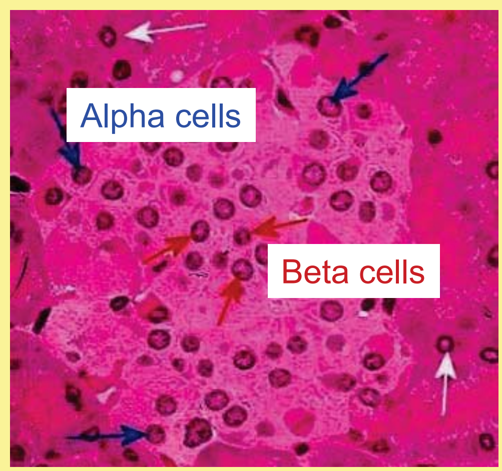
-- numerous 300nm cytoplasmic granules with an eccentrically placed electron dense core.



-- Alpha cells secrete a 29 amino acid peptide ***GLUCAGON,*** which act to raise blood glucose levels by promoting the formation of glucose from glycogen stored in the liver (glycogenolysis)



2. BETA CELLS: (70%)



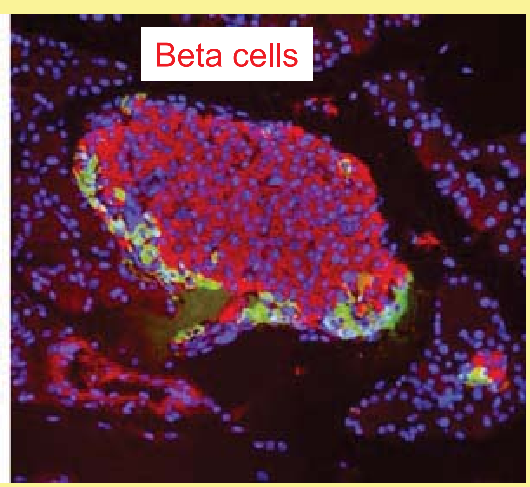
-- small cells - most numerous

-- tend to be concentrated in the center of the islets

-- contain 300nm vesicle which have an electron dense core surrounded by a less dense matrix

Beta cells secrete the hormone *INSULIN,* which acts to regulate blood glucose levels in 2 ways:

1. **promoting glucose transfer from plasma into target tissues.**
2. **stimulating the conversion of glucose to glycogen in liver hapatocytes**



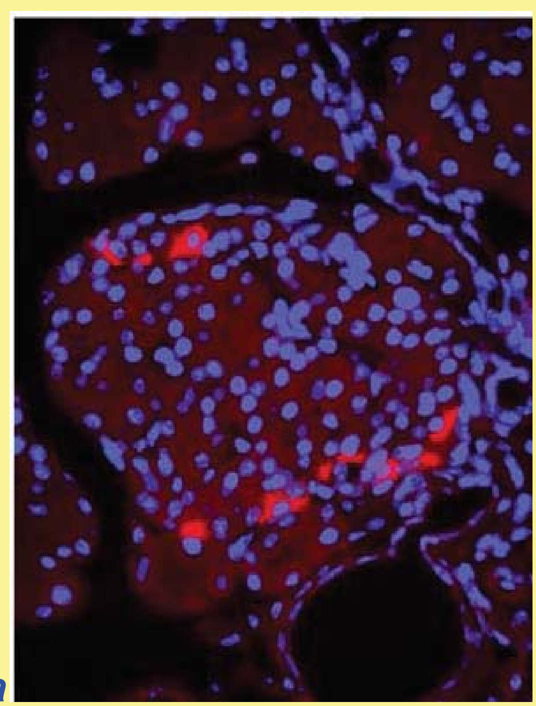
Defects in insulin function results in a clinical condition known as DIABETES MELLITUS characterized by:

1. **<u>hyperglycemia</u> due to decreased tissue uptake of glucose from the blood**
2. **increased glucose in the urine <u>(glucosuria)</u>**
3. **increased excretion of water <u>(polyuria)</u>**

- **Early onset - (type 1) diabetes is usually associated with <u>reduced Beta cell secretion.</u>**
- **Adult onset - (type 2) diabetes more commonly results from a <u>defect in insulin receptors</u>.**

3. <u>DELTA CELLS</u> (5%)

-- larger than Alpha and Beta cells
-- numerous <u>lightly electron dense</u> secretory vesicles of varying size
-- Secrete a 14 amino acid peptide, SOMATOSTATIN



Somatostatin acts as both a <u>neurotransmitter</u> and a <u>neurohormone</u> in different tissues

1. ***in the hypothalamus somatostatin =***

   growth hormone release

2. ***in the pancreas this hormone acts in a paracrine fashion to***

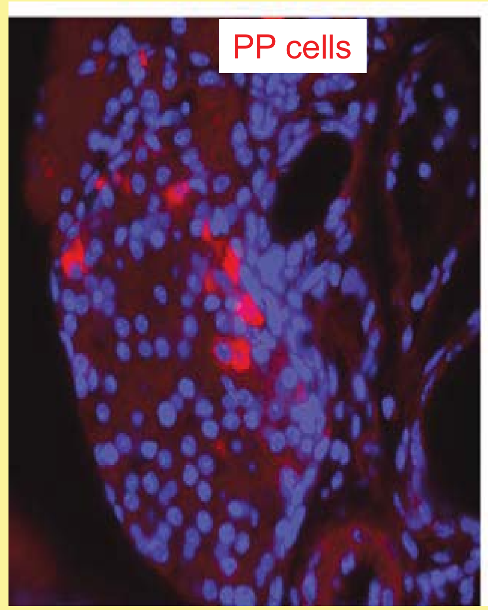
   <u>glucagon and insulin release</u>

4. <u>F- CELLS</u> (PP cells) (5%)

-- not much is known about these cells

-- their secretory vesicles contain a 36 amino acid peptide called PANCREATIC POLYPEPTIDE which appears to:

1. stimulate the release of gastric secretions in the gut
2. inhibit bile secretion in the gall bladder



5. G-cells: (??)

Little is known about these cells.

- only present during maturation.

-- 1% cell - scattered throughout islets

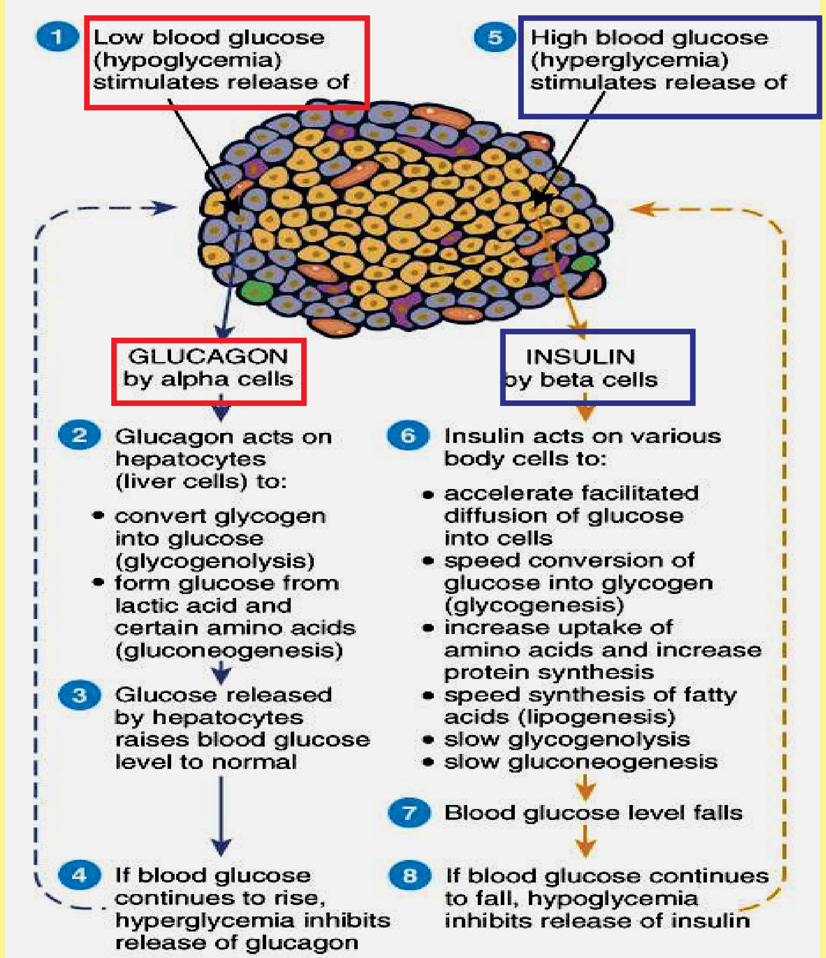
G-cells secrete GASTRIN which:

-- increases HCL secretion in the stomach

-- increases gastric motility

- A, B and D cells are connected by gap junctions and their secretions can be influenced by local diffusion(PARACRINE) effects.

Glucagon & Insulin release are regulated by plasma glucose levels.



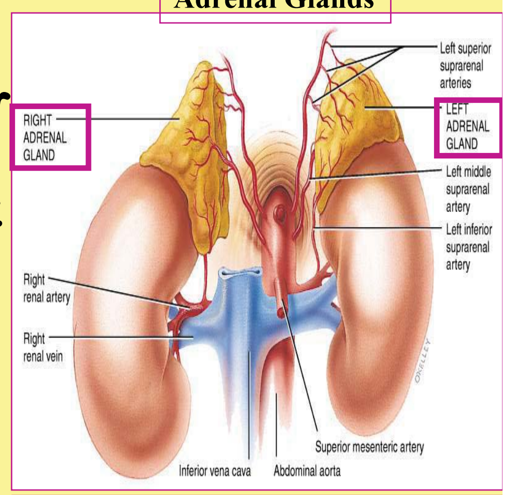
THE ADRENAL GLANDS

The Adrenal glands consist of a pair of flattened, creascent- shaped glandular masses 5 X 4 x 3 cm, that lie at the superior-medial border of the kidneys.

Each gland weighs approx 6-8 gm making the adrenals one of the largest endocrine organs.

The adrenal consists of two concentric layers of tissue covered by a thick fibroelastic connective tissue capsule endowed with a rich vascular supply.

Adrenal Glands



- One on top of each kidney
- Cortex produces 3 different types of hormones from 3 zones of cortex

-Medulla produces
-epinephrine & norepinephrine

The adrenal gland is divided into 2 layers:

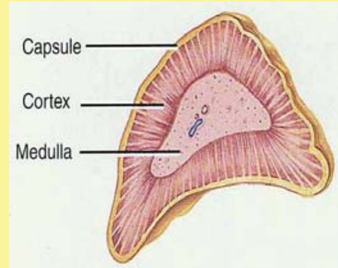
-- a yellow peripheral layer = the **ADRENAL CORTEX** (80%)

-- a central reddish-brown layer = the **ADRENAL MEDULLA** (20%)

These layers <u>can be considered as 2 separate endocrine tissues</u> that differ in:

1. embryological origin
2. type of hormonal secretion
3. function

Structure of Adrenal Gland

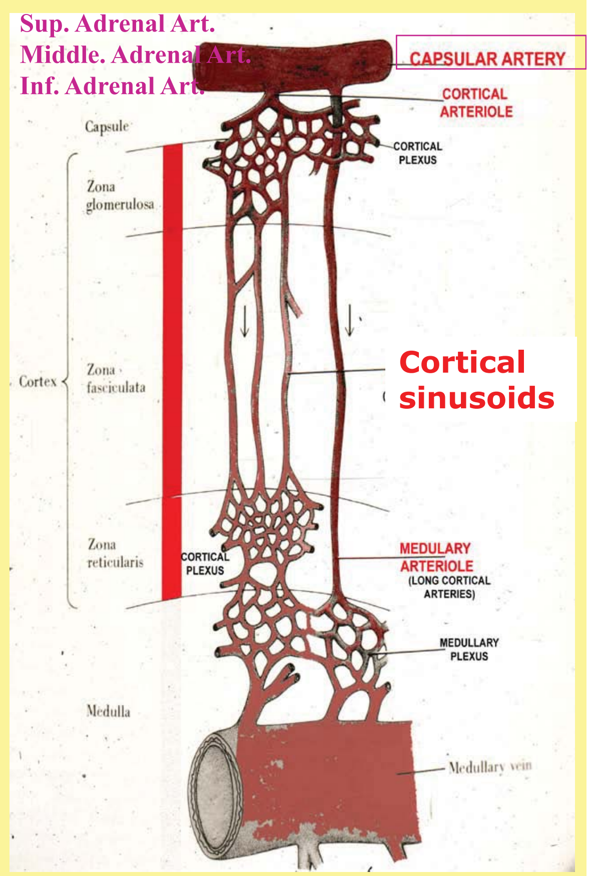


- Cortex derived from mesoderm
- Medulla derived from ectoderm

The adrenal gland receives a **rich vascular supply**.
Blood is supplied to the gland from <u>three main groups of arteries:</u>

1. **superior adrenal art.** - arising from branches of the inferior phrenic art.
2. **middle adrenal art**. - originating from the aorta
3. **inferior adrenal** - arising from the renal art.

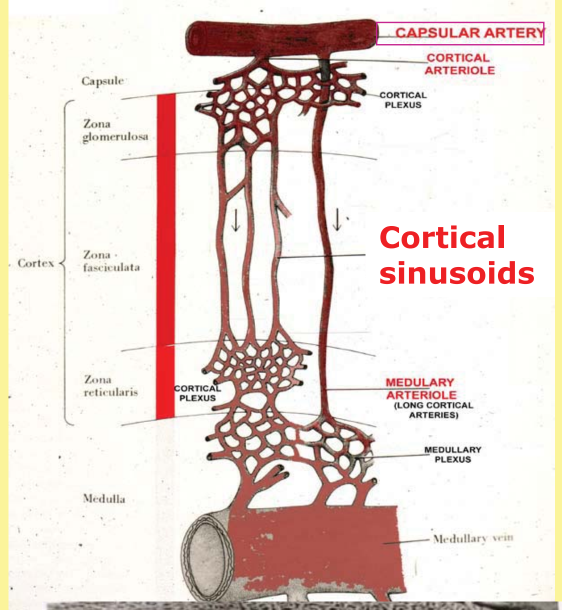
These arteries branch in the outer capsule of the gland to form the ***CAPSULAR ARTERIES***

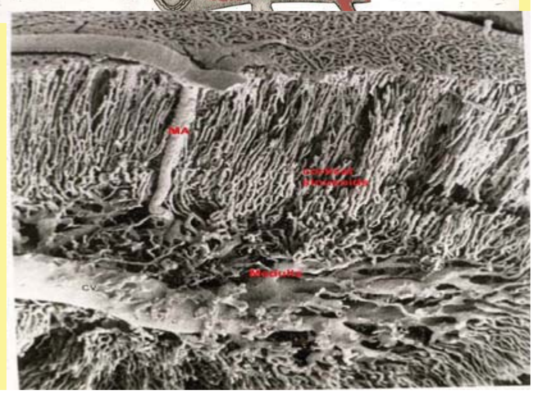


The Capsular Arteries penetrate the parenchyma of the gland where they branch extensively to form:

1. cortical arterioles which give rise to:
   - capillary plexus of the cortex (zona glomerulosa)
   - cortical sinusoids
2. medullary arterioles
   - capillary plexus of the medulla

Capillaries in the adrenal gland are fenestrated sinusoid like other endocrine organs





THE ADRENAL CORTEX

Cells of the parenchyma consist of secretory epithelium supported by network of reticular fibers.

The cortex is encapsulated by a thick FIBROELASTIC CONNECTIVE TISSUE capsule whose trabeculae penetrate the tissue carrying nerves and blood vessels

The secretory epithelium elaborate a wide variety of Steroid Hormones which can be classified into three major categories:

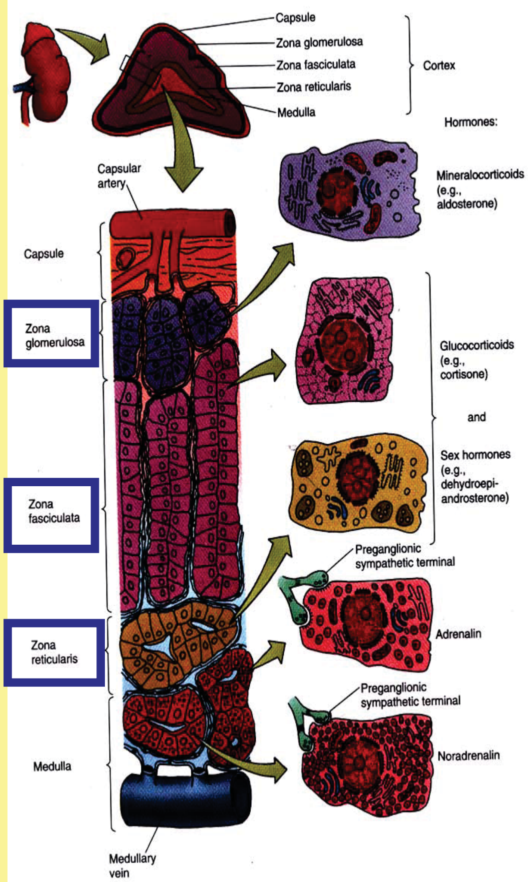
1. Glucocorticoids (effect carbohydrate metabolism)
2. Mineralocorticoids (effect fluid and electrolyte balance)
3. Gonadal Steroids (effects similar to hormones secreted by the testis)

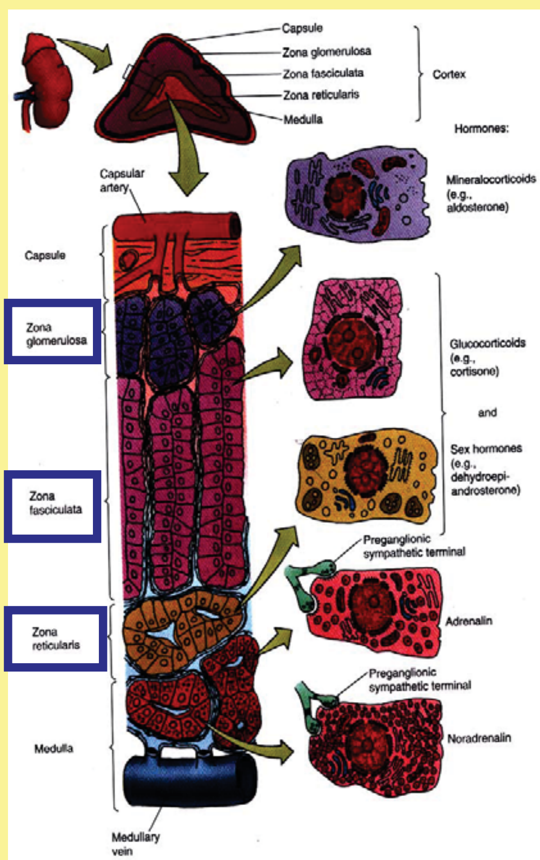
Secretion of adrenocortical hormones is controlled by the release of ACTH from basophils in the anterior pituitary and by the renin/angiotensin system

In nearly all mammals the adrenal cortex can be divided into three concentric zone based on the arrangement of the secretory epithelial cells:

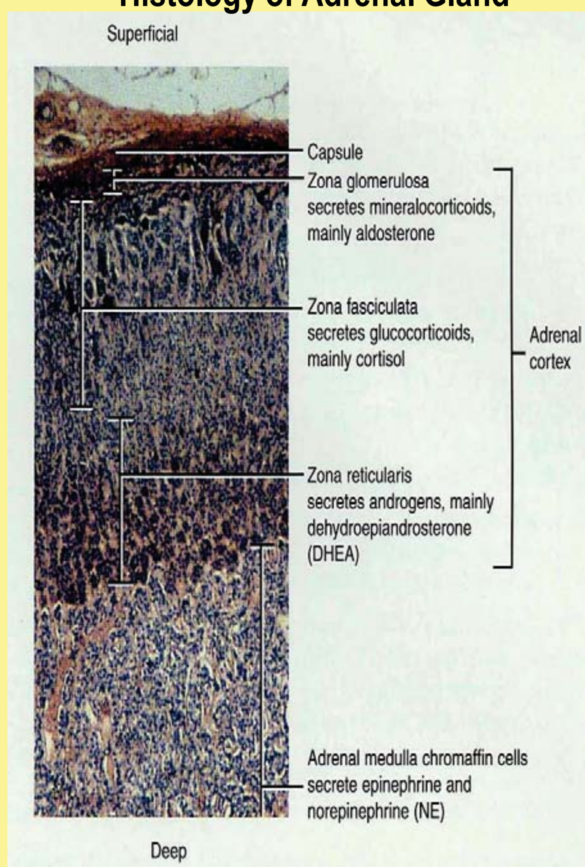
1. **thin outer Zona Glomerulosa (15%)**
2. **thick middle Zona Fasciculata (78%)**
3. **thin inner Zona Reticularis , adjacent to the medulla (7%)**

The transition between zones is gradual and the boundaries are indistinct.





Histology of Adrenal Gland



ZONA GLOMERULOSA

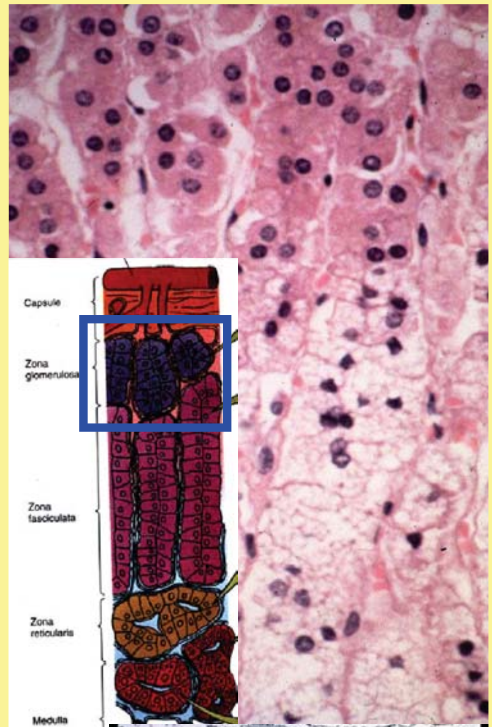
This zone lies immediately beneath the capsule of the gland

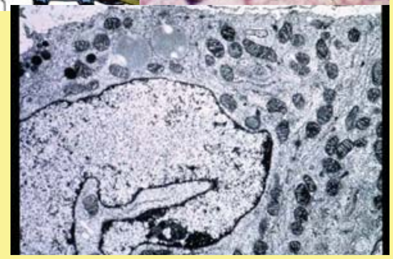
consists of small pyramidal or columnar cells (12-15um) arranged in spherical aggregates surrounded by capillaries

cells have large deeply staining spherical nuclei, homogeneously staining cytoplasm

At the EM level:

-- well developed smooth ER, numerous mitochondria with lamellar cristae.





Zona Glomerulosa cells secrete 2 major *MINERALOCORTICOID HORMONES* which play an important role in the maintenance of water and electrolyte balance.

1. *ALDOSTERONE*
2. *DEOXYCORTICOSTERONE*

Mineralocorticoids act to promote the resorption of Na+ from:

- the distal convoluted tubules of the kidney
- sweat glands and salivary glands.

Their secretion is controlled primarily by the renin/angiotensin system but also responds to stress-related release of ACTH

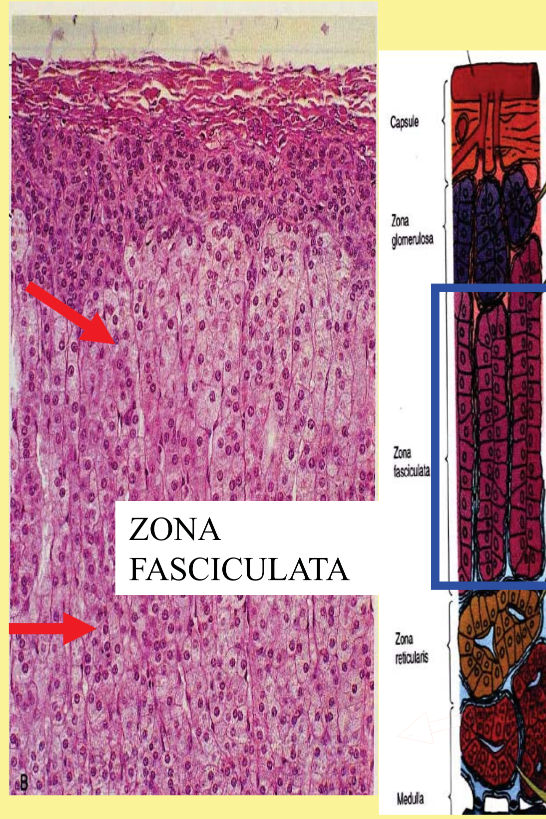
ZONA FASCICULATA

This is the thickest zone of the adrenal cortex composed of long radially oriented cords of secretory epithelial cells separated by capillaries

cells are larger than in the Glomerulosa (approx. 20µm) and exhibit centrally located vesicular nuclei, often binucleated.

cytoplasm is lightly basophilic with numerous lipid droplets containing fatty acids, cholesterol and neutral fat.

The apical cytoplasm has short microvilli that extend into the capillary sinusoids and numerous mitochondria



Zona Fasciculata cells synthesize and secrete ***GLUCOCORTICOIDS*** principally ***CORTISOL*** **(also some cortisone and corticosterone)** whose principal actions are:

1. **down-regulation of the immune response** by inhibition of lymphocyte production and turnover

2. **modulation carbohydrate metabolism** by promoting the formation of glucose from protein

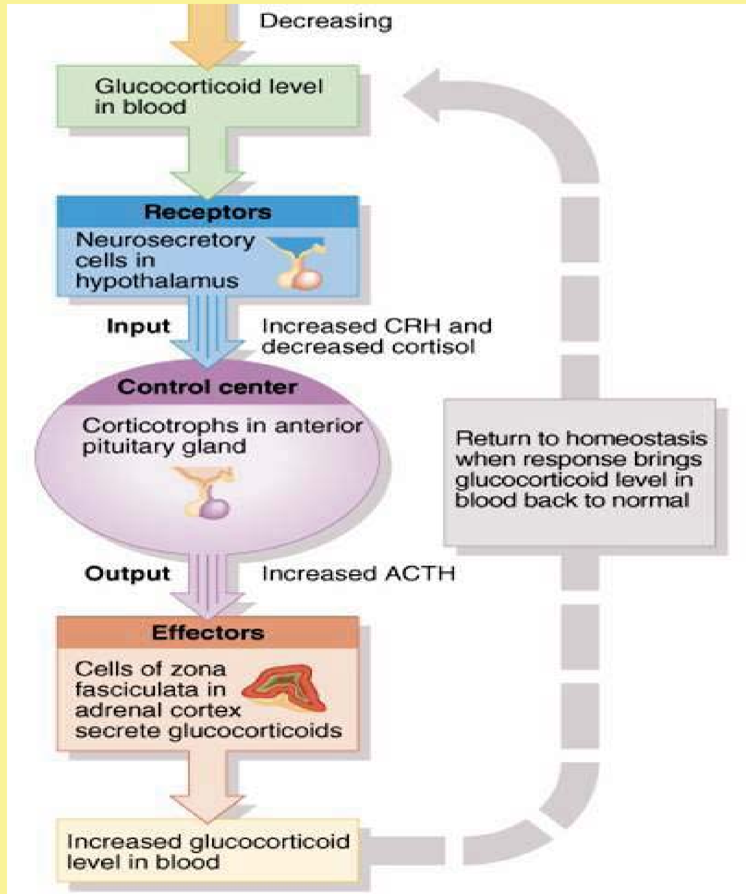
3. **suppression of inflammatory response** by decreasing production of T-cells and Plasma cells

Regulation of Glucocorticoids

Cortisol release is under negative feedback control from:

A. corticotrophs in the anterior pituitary (via ACTH release)

B. hypothalamic neurosecretory cells which release CRH



ZONA RETICULARIS

thinnest innermost zone of secretory epithelial cells– irregularly anastomosing cords separated by sinusoids

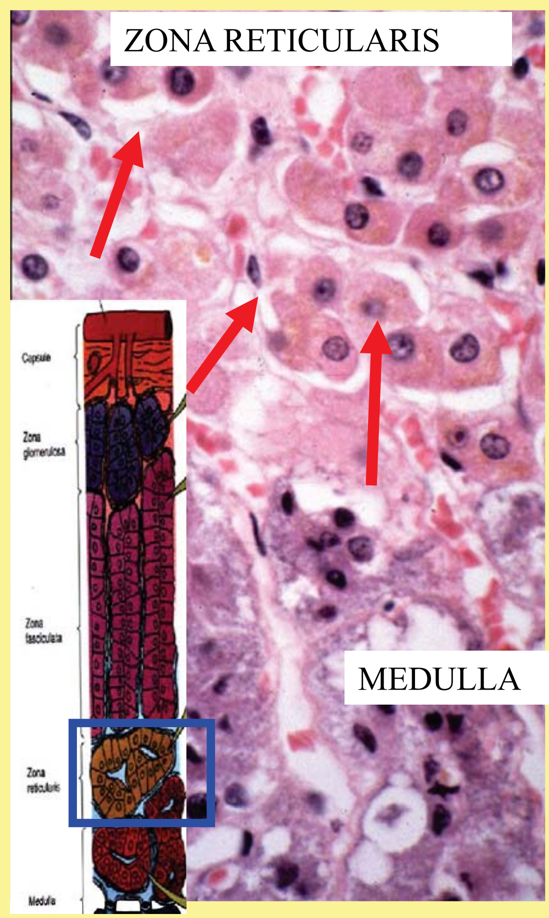
Cell smaller than those of the fasciculata (12-14 µm), with deeply staining nuclei

Few lipid droplets evident in cytoplasm, but numerous secondary lysosomes as well as lipofuscin pigment granules.

Zona Reticularis cells secrete:

1. residual amounts of cortisol (like the zona fasciculata)

2. several weak steroidal *ANDROGENS* (these do not appear to be stored in vesicles, but continuously released)



The amounts of androgen released by the zona reticularis cells are not significant under normal physiological conditions

S <u>tumors of these cells can develop causing release of large amounts of adrenal androgens</u>.

S In prepubertal males such tumors can result in
-- precocious development of the sex organs
-- secondary sexual characteristics

S In females = Adrenogenital Syndrome

-- androgenization of genitalia
-- development of male 2nd sexual characteristics
-- in extreme cases; pseudohermaphroditism

ADRENAL CORTEX DYSFUNCTION:

ADDISON'S DISEASE:

primary HYPOadrenalism - idiopathic atrophy of the adrenal cortex

-- weakness and drowsiness due to low blood glucose (glucocorticoids)

-- increased ACTH secretion

-- decreased blood pressure due to decreased extracellular fluid volume (mineralocorticoids)

-- decreased absorption of Na+ and Cl- ions in kidneys

Addison's Disease (hypoadrenalism)

- fatigue
- weakness
- low blood pressure
- darkening of skin

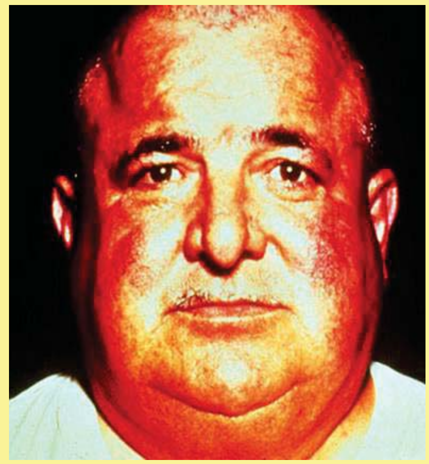
CUSHINGS DISEASE

HYPERadrenalism {adrenal cortical tumors}

- -- can result from excessive synthetic glucocorticoid use
- -- redistribution of fat around the neck, face ("moon face") and abdomen
- -- wasting of limb musculature, and thinning of bones due to antianabolic effects of glucocorticoids on protein synthesis in these tissues
- -- thinning of skin, and loss of fat in the hypodermis causes underlying blood vessels to show through
- – hyperglycemia

Cushing's disease (hyperadrenalism)

-"Moon face"
- muscle wasting
- skin thinning



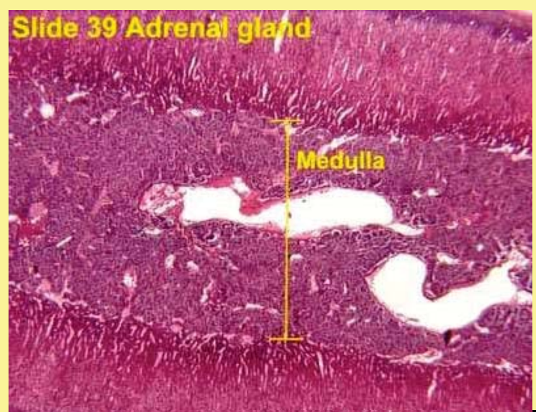
THE ADRENAL MEDULLA

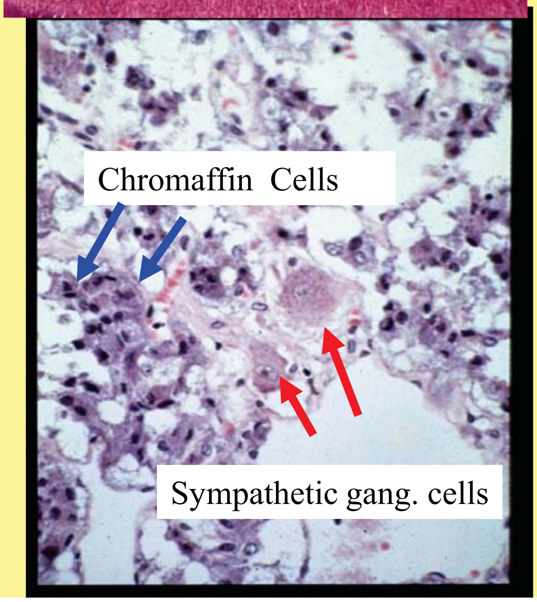
Composed of large ovoid pale staining cells called *CHROMAFFIN CELLS* arranged in irregular clumps or cords between wide fenestrated capillaries

Cell are supported by reticular fibers

Chromaffin cells are derived from sympathetic ganglion cells of the celiac plexus which migrate into the adrenal cortex.

These are basically neurons which have lost their axonal and dendritic processes and function as secretory cells.





these cells receive direct cholinergic synapses from preganglionic sympathetic fibers of the autonomic nervous system, which play a major role in controlling their secretions (splanchnic nerve)

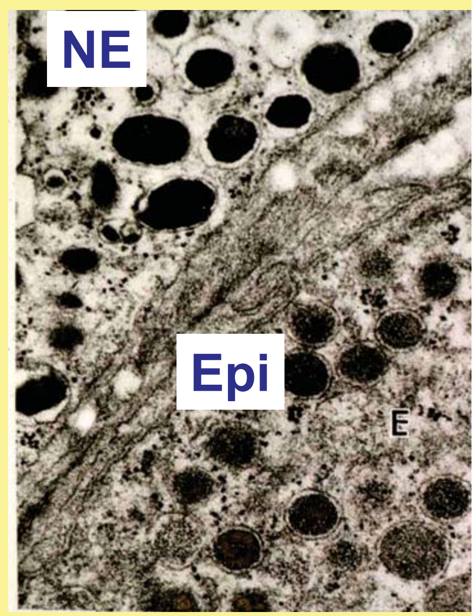
scattered postganglion sympathetic neurons can often be found in sections through the adrenal medulla

The cytoplasm of Chromaffin cells exhibits membrane bound dense core secretory granules (200-300nm) which contain catecholamines.

2 types of catecholamine secreting cells have been distinguished via immunocytochemistry:

1. Epinephrine cells (80%) -- round moderately electron dense granules which fill the vesicles. These cells tend to cluster around the adrenal sinusoids.

2. Norepinephrine cells (20%) -- flattened or ovoid granules with eccentrically located high electron dense core surrounded by a less electron dense ring. these cells tend to cluster around the adrenal arterioles.



The differential clustering of these 2 cell types is related to the synthesis of the hormonal product

– Epinephrine is synthesized from norepinephrine via the addition of a methyl group. The enzyme that catalyzes this transformation is "glucocorticoid induced".

Those cells closest to the sinusoids

S are bathed in glucocorticoids from the adrenal cortex, and their norepinephrine will is processed into epinephrine.

S cells further away from the sinusoids are not exposed to glucocorticoids and their norepinephrine will not be processed into epinephrine.

Release of catecholamines from adrenal medulla cells results from neural impulses in their preganglionic fibers. This process is Ca+ dependent.

CATECHOLAMINE FUNCTION:

Catecholamines release is controlled by the sympathetic branch of the autonomic nervous system in response to environmental and emotional stresses.

Catecholamines reinforce the actions of the sympathetic nervous system in preparation for dealing with the stress:

-- elevate plasma glucose levels (stimulate glycogenolysis)

-- increase blood pressure and cardiac output

-- dilation of coronary and skeletal muscle blood vessels

-- cutaneous vasoconstriction